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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,292	03/10/2004	Kunwar Shailubhai	122069-40308707	9377

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,292	SHAILUBHAI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,21-23,25-30,32 and 34-38* is/are rejected.

7)☒ Claim(s) *24, 31 and 33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 10/25/05; 4/13/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II claims 11-12 and newly added claims 21-38 in the reply filed on February 7, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant specifically elected among list of disease-malignant carcinoid with a specific compound N,N-dimethyl-8-8-dipropyl-2-azaspiro[4,5]decane-2-propanamine dimaleate. Examiner has withdrawn the specie election of malignant carcinoid and extended to include previously non-elected species as cited in the below prior art references, however not all of the non-elected specie are examined.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 10/25/05 and 4/13/06 has been acknowledged. The information disclosure statement filed fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because items C1 and C6 of the above IDS, 10/25/05 and 4/13/06 are either not a publication. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all

certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Allowable Subject Matter

Claims 24, 31 and 33 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those

in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The nature of the invention: The claim is directed to a method of treating cancer comprising administering to a mammal a therapeutically effective amount of a N,N-dimethyl-8,8-dipropyl-2-azaspirol[4,5]decane-2-propanamine dialeate. From reading the specification, a wide variation of cell lines have been taught (see pages 22-23) for cell lines and in vivo pages 26-30).

the state of the prior art: The state of the prior art is that cancer therapy remains highly unpredictable, which Applicant is aware of (see specification para 0004) The various types of cancers have different causative agents involve in the cellular mechanism, and consequently, differ in treatment protocol. It is known (see Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537) that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, to maximize efficacy and minimize toxicity. Cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of skill in the art from accepting any therapeutic regimen on its face as already discussed in para 0004 of the specification.

the amount or direction presented, the presence or absence of working examples; Although a wide claim to a vast variation of cancer treatment has been shown in the specification, it however, fails to show how one such compound is capable of treating these wide variation of cancer. Noted these treatment are to cell lines, and animal models, Applicant has failed to show how these data is extrapolated for human studies No supporting evidence have been provided.

The level of the skilled artisan: Even though the level of skill in the pharmaceutical art is very high, based on the" unpredictable nature of the invention and state of the prior art and lack of guidance and direction, one skilled in the art could not use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims11-12, 21-22, 25-30, 32, 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rice et al. J. Heterocyclic Chem., 10(5):731-735 (1973) (applicants prior art submission) taken with Mirabelli et al. Anti-Cancer Drug Design, 3(4):231-242 (1989) (also Applicant prior art submission) in view of Badger et al. US 5,602,166 and Dagger et al. US 5,939,450.

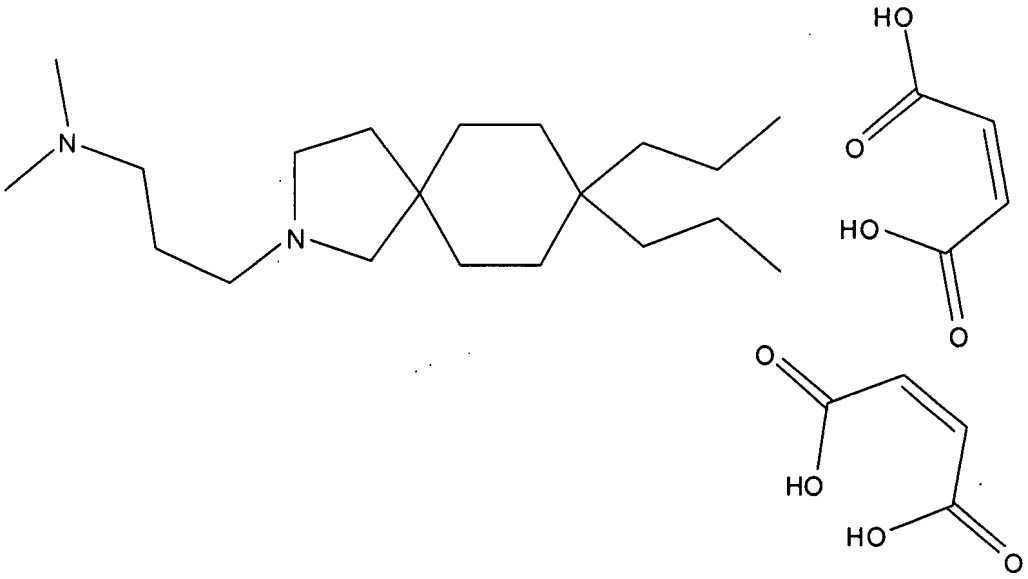
Rice et al. teach the drug N,N-dimethyl-8,8-dipropyl-2-azaspirol[4,5]decane a member of the class of drugs azaspirane (see abstract) for the treatment of cancer where in the drug showed a significant inhibition of cancer cell growth in human cancer cells.

Mirabelli et al. teach structurally related azaspiranes in the treatment of cancer, wherein N,N-dimethylaminopropyl-2-aza-8,8-diethyl-8-germaspiro[4,5]decane is used together with other chemical drugs that are obvious variation of the claimed drug in the instant claim 11 was used to determine in vitro and in vivo activity (see page 234) as in the instant claim 11-12, wherein the cancer is a mammary adenocarcinoma (Mammary

adenocarcinoma are cancers that begins in cells that line the inside of organs. They begin in cells that make milk) as evident by breastcancer.org (2001). The reference Mirabelli et al. teach breast cancer, and prostate cancer (see page 231) as in claim 12, wherein the cancer is breast, prostate (see page 231) and colon cancer (see page 232) as in claims 32, 34-35 and 38. With regards to claims 12, 21-22 and 37 regarding the structure, Applicant should note that a specie election has been made and the compound elected is the result of the varying substituents of R.

Badger et al. teach N,N-dimethyl-8-8-dipropyl-2-azaspiro[4,5]decane-2-propanamine is a cytokine inhibitor. Cytokines have been found to play a major role in the control of estrogen in breast cancer. As evident by Nakshatri et al, showed cytokines induce nuclear factor-κB (NF-κB) identified IL-1 as the factor responsible for NF-κB activation of fibroblast. Analysis of the primary breast carcinomas showed the presence of IL-1 transcriptase in the majority of lymph node-positive breast cancer. Therefore the teaching of Badger would have resulted in using the compound N,N-dimethyl-8,8-dipropyl-2-azaspirol[4,5]decane-2-propanamine salt for the treatment of breast cancer in humans (see abstract and see col. 6, lines 54-55) as in claim 26, but fail to teach the dimaleate salt, wherein the drug is administered orally or parenterally (see col. 6, lines22-23) as in claims 27-28) in the amount of 0.1 mg-100/kg mg per day (see col. 6, lines 29-35) to a human (see col. 6, line 6) as in claims 29-30). The

compound elected is



3-(8,8-dipropyl-2-azaspiro[4.5]decan-2-yl)-*N*,*N*-dimethylpropan-1-amine dimaleate

and would have resulted from the compound of formula I (see col. 2, lines 3-30). Note that R (1-2) are straight chain alkyl, R(3-4) are the same containing one carbon atom- a methyl group. (The maleate form of the compound was taught by US 5,939,450 by Dagger et al. see col. 1, lines 8-25) where the exact compound is taught.

Although, the Rice et al. reference, fail to use the exact compound of the above structure, one of ordinary skill in the art would have been motivated to make and use the dimaleate form of the class of compounds as taught by Dagger et al. and use for the treatment of cancer in general as taught by Rice. Even though, no specific cancer type was taught, the generic teaching would suggest to one of ordinary skill in the art to make and use for the treatment to treat breast, colon and prostate cancer because Mirabelli et al. used compounds of azaspirane to treat these types of cancer. The drug

of above structure falls in the class of azaspirane. Therefore one of ordinary skill in the art would be motivated to switch the compound of Rice et al. or Mirabelli et al. to the compound of Dagger et al. treat colon, breast and prostate cancer and expect a successful result in doing so because the art has used close structural similarity (homologs) of the reference compound for the treatment of these cancers.

Claims 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rice et al. J. Heterocyclic Chem., 10(5):731-735 (1973) (applicants prior art submission) taken with Mirabelli et al. Anti-Cancer Drug Design, 3(4):231-242 (1989) (also Applicant prior art submission) in view of Badger et al. US 5,602,166 and Dagger et al. US 5,939,450 as applied to claims 11-12, 21-22, 25-30, 32, 34-38 further in view of Gnaidecki et al. Expert Opinion Emerging Drugs (2002) 7(1) 69-90 taken with Victor J. Drugs in Dermatology 2002 1-15.

Gnaidecki et al. teach Atripod dimaleate has been used in combination treatment. (see page 80) for the treatment of psoriasis.

Victor teach, cytokine in innate response in psoriatic lesions. That Tumor necrosis factor (TNF-alpha increases production of pro-inflammatory cells IL-1 etc (see abstract). As taught above by Badger et al, Atripod dimaleate inhibits cytokine IL-1, therefore if cytokine-IL-1 is inhibited in a psoriatic lesion, one would expect the same inhibition to take place in breast cancer.

Although, the reference did not teach any particular drug, only suggest that it has been considered in a combination therapy for the treatment of psoriasis, one of ordinary

skill in the art would be motivated to use a potentiating agent with the drug, especially another chemotherapeutic drug for the treatment of cancer, because (as Goodman and Gillman teach various class of chemotherapeutic drugs have been combined with small molecule cancer drugs for a synergistic effect in treating cancer (see as evident by Goodman et al pg, 1225, 1227 and 1230 as combination therapy are generally more effective through their biochemical interactions. (see 1230 underlined sec.). Thus nothing is unobvious is seen in combining a chemotherapeutic with the azaspirane as taught adjuvant therapy is a routine for the treatment of cancers such as breast, colon (see 1225).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
5/4/07

Ardin H Marschel 6/11/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER